Remarks

Claims 21-29 are pending. Claims 21, 22, 23 and 26 have been amended. Claims 1-20 have been canceled. Claims 21, 22 and 26 were amended to provide clarity. Support for the amendments can be found, for example, at page 3, lines 6-8 (genes encoding proteins); page 6, lines 17-19 (reacting primers with genes and primers having lengths of 480-700 base pairs); and page 11, lines 11-14 (arraying amplicons). Claim 23 was amended to correct minor typographical errors. Claims 21-29 define an improved microarray screening method, wherein the primers are selected to bind to non-consensus sequence so that non-specific binding is minimized. The claims are drawn to regulatory-sequence based gene microarrays comprosed nucleic acid sequences of genes whose non-coding region contains the same defined nucleotide bases for enhancers or repressors to bind to; and genes whose protein products can bind to designated regulatory sequences (E-box sequences).

The present invention is directed to regulatory-sequence based gene microarrays composed of genes ***whose non-coding region contains the same defined nucleotide bases for enhancers or repressors to bind to; and genes whose protein products can bind to designated E-box regulatory sequences***. There are many examples of such regulation occurring in cells, and promotion of a specific cellular event usually requires the concerted and coordinated activation of a group of genes. The claimed invention contrasts with the currently available DNA microarray technology which is based on screening the coding sequences of thousands of genes, many of which may only be "ESTs" of unknown function. The claimed technology is

based on designing a specific subset of genes ***whose expressions are regulated by the same regulatory mode, i.e. the activation of gene expression based on the activation or deactivation of defined DNA sequences (i.e. E-box regulatory sequences).***

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 21-29 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The applicants have amended claim 21 to provide a nexus between the preamble and the claim steps. Claims 21, 22 and 26 were amended to clarify the interactions between reagents within the methods.

Rejection Under 35 U.S.C. § 102

Claims 22-23 and 25-29 were rejected under 35 U.S.C. § 102(b) as being anticipated by by Nature Genetics 14(4):457-460 by DiRisi *et al.* ("DiRisi"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

DiRisi teaches the assessment of mRNA levels in cell lines *via* the hybridization of cDNA probes generated from single oligo dT-selected mRNA pools (prepared from mRNA by oligo dT-primed polymerization; see Methods, page 459). Furthermore, DeRisi teaches DNA microarrays, containing 1,161 total elements, including 870 different cDNAs and controls. However, DeRisi fails to teach or suggest a critical step in the presently claimed method: providing genes that are under the control of the same E-box regulatory element/or have

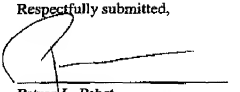
common E-box regulatory sequences. As discussed above, the design of regulatory-sequence based gene microarrays is a rationale strategy in gene screening, allowing the results gained to immediately applied as a reflection of a regulatory pathway, rather than random hit-or-miss gene screening.

Claims 22, 24-28 and 34-37 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,524,800 to Lockhart *et al.* ("Lockhart"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Lockhart teaches the characterization of cellular effects of potentially therapeutic compounds on a genome-wide scale by monitoring changes in messenger RNA levels in treated cells with high density oligonucleotide probe arrays (see abstract). Lockhart is a perfect example of methods being used to screen thousands of coding sequences. As discussed above, results obtained from such large screens provide only a general sketch of which gene expressions are gained or lost in a specific physiological condition. Lockhart does not even teach a grouping of genes based upon their functional capability, such as cell proliferation, cell cycle apoptosis, DNA repair. Lockhart is in complete contrast to the presently claimed methods, wherein genes are grouped according to their regulatory modalities (i.e. genes whose expression is dependent upon E-box regulatory sequences or genes that encode proteins or cofactors that bind to the E-box regulatory sequence).

Allowance of claims 21-29 is respectfully solicited.

Respectfully submitted,



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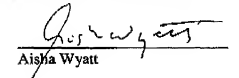
I hereby certify that this Amendment and Response to Office Action, and any documents referred to as attached therein are being facsimile transmitted on this date, July 3, 2003, to the Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.



Aisha Wyatt

Date: July 3, 2003

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